DISCLOSURES

- I do not have any relevant financial disclosures.

OBJECTIVES

- Understand the impact of glycemic control on clinical outcomes for noncritically ill medical and surgical patients
- Review current guidelines and glycemic targets for noncritically ill patients
- Review strategies for safe and effective glycemic control from admission until discharge
- Discuss challenges to glycemic control unique to the hospital setting
HYPERGLYCEMIA: A COMMON COMORBIDITY IN MEDICAL-SURGICAL PATIENTS IN A COMMUNITY HOSPITAL

- Normoglycemia: 62%
- Known history of diabetes: 26%
- Newly discovered Hyperglycemia: 12%

n = 2,020


HYPERGLYCEMIA IS AN INDEPENDENT MARKER OF INPATIENT MORTALITY IN PATIENTS WITH UNDIAGNOSED DIABETES

- In-hospital Mortality Rate (%)
  - Patients With Normoglycemia: 2%
  - Patients With History of Diabetes: 3%
  - Newly Discovered Hyperglycemia: 16%

P = 0.01


THE IMPACT OF HYPERGLYCEMIA IN NONCRITICALLY ILL PATIENTS

- New study on the impact of hyperglycemia in noncritically ill patients.
INPATIENT HYPERGLYCEMIA HAS BEEN SHOWN TO BE A MARKER OF POOR OUTCOMES...

- Critical Illness: ICU, cardiothoracic surgery, acute myocardial infarction
- Surgery: orthopedic, vascular, colorectal, bariatric, trauma
- Medical: COPD exacerbation, pneumonia
- Neurology: Stroke, Cerebral Aneurysm, Subarachnoid Hemorrhage
- Obstetrics: Labor and Delivery

INCREASED WOUND AND NOSOCOMIAL INFECTIONS

Perioperative Glycemic Control and the Risk of Infectious Complications in a Cohort of Adults with Diabetes*

<table>
<thead>
<tr>
<th>Relative Odds of Wound Infections</th>
</tr>
</thead>
<tbody>
<tr>
<td>121-206</td>
</tr>
<tr>
<td>207-229</td>
</tr>
<tr>
<td>230-252</td>
</tr>
<tr>
<td>253-353</td>
</tr>
</tbody>
</table>

(P < 0.05 for upward trend)

Early postoperative glucose control predicts nosocomial infections rate in diabetic patients.

Relative risk for “serious” post-op infections increased to 5.7 when glucose >220 mg/dL


IN-HOSPITAL COMPLICATIONS WITH AND WITHOUT DIABETES IN NONCARDIAC SURGERY

Thirty-day mortality and in-hospital complication rates in patients with and without diabetes: blood infection (combined bacteremia and sepsis), urinary tract infection (UTI), acute myocardial infarction (AMI), and ARF. "P < 0.001; NS: "P > 0.051.

Frisch, A et al. Dia Care.1999;23:178-1798
**IMMEDIATE PRE-OP GLUCOSE AND MORTALITY**

- Case controlled study of 2151 patients who underwent elective non-cardiac surgery
- Pre-op random glucose measurements defined as:
  - Normal: < 110 mg/dL
  - Pre-DM: 110-200 mg/dL
  - DM: > 200 mg/dL
- Prediabetes: 1.7 fold increased mortality compared to normal
- Diabetes: 2.1 fold increased mortality


**ASSOCIATION OF MEAN GLUCOSE BEFORE AND AFTER NONCARDIAC SURGERY**

Patients WITHOUT diabetes had higher odds ratio of 30 day mortality with higher mean glucose levels

- All patients
- Patients with Diabetes
- Patients without Diabetes

Frisch, A et al. Dia Care 2010;33:1783-1788

**PRE-OP GLYCEMIC CONTROL - ORTHOPEDICS**

- 115 patients with Type 2 DM s/p TKA
  - Preoperative HgA1c ≥ 8% was an independent risk factor of wound complications (OR 6.07)
- Duke Study: >1 million patients who underwent joint replacement surgery from 1988-2005
  - Uncontrolled diabetes had higher adjusted odds ratio of:
    - Stroke (OR 3.42)
    - UTI (OR 1.97)
    - Postop hemorrhage (OR 1.99)
    - Wound infection (OR 2.28)
    - Ileus (OR 1.99)
    - Death (OR 3.23)


10/11/2016
COLORECTAL AND BARIATRIC SURGERY WITH POSTOPERATIVE GLUCOSE >180 MG/DL

N=11,633

Outcomes stratified by perioperative hyperglycemia (>180 mg/dL at any point on the day of surgery, postoperative day 1, or postoperative day 2) for diabetic patients (A) and nondiabetic patients (B).


EARLY (48H) POSTOPERATIVE GLUCOSE LEVELS AND SSI AFTER VASCULAR SURGERY

P for trend=0.003; *P=0.006; **P=0.28; ***P=0.69

Adapted from Vriesendorp. Eur J Vasc Endovasc Surg 2004; 28:520-5

HYPERGLYCEMIA AND STROKE

A: Predicted probability of in-hospital adjusted mortality
B: Predicted probability of adjusted symptomatic intracranial hemorrhage

Shihab Masrur et al. J Am Heart Assoc 2015;4:e002193
GUIDELINES FOR HYPERGLYCEMIA MANAGEMENT OF NONCRITICALLY PATIENTS

MANAGEMENT WITH SLIDING-Scale INSULIN IS INADEQUATE

- Reactive therapy → provides supplemental insulin after hyperglycemia occurs
- No basal (long term) insulin coverage:
  - Will cause DKA in patients with Type 1 diabetes
- Does not consider nutritional changes or diurnal insulin requirements
- Non physiologic dosing that results in:
  - Increased incidence of hyperglycemic and hypoglycemic episodes

Queale WS et al. Arch Intern Med. 1987;147:345-352

ROLLER COASTER EFFECT OF SLIDING-SCALE INSULIN

Glucose

Time
• 130 insulin naïve patients with Type 2 diabetes
• Discontinued all oral antidiabetic drugs on admission
• Randomized to:
  - Basal-Bolus Arm: glargine and glulisine
  - Standard Arm: Sliding Scale Insulin alone

Starting Total Daily Dose (TDD):
- 0.4 units/kg/d x BG between 140-200 mg/dL
- 0.5 units/kg/d x BG between 201-400 mg/dL
- Half as glargine and half as glulisine divided daily with meals

*P<0.05

Sliding scale regular insulin (SSRI): given 4 times daily. Basal-bolus regimen: glargine once daily; glulisine before meals. 0.4 U/kg/d x BG between 140-200 mg/dL. 0.5 U/kg/d x BG between 201-400 mg/dL.

Failure was defined as 3 consecutive BG values > 240 mg/dL during SSRI
RABBIT-2 SURGERY: BASAL-BOLUS INSULIN THERAPY HAS LOWER POSTOPERATIVE COMPLICATIONS

- Results:
  - Daily blood glucose (BG):
    - Lower mean fasting, lower mean daily glucose more glucose readings < 140 mg/dl
  - Reduced composite endpoints of postoperative complications:
    - Reduced at 8.6 % vs. 24.3% (P=0.003)
    - Wound infection: 2.9 vs. 10.3% (P=0.247)
    - Pneumonia: 0 vs. 2.8% (P=0.247)
    - Acute renal failure: 3.8 vs. 10.3% (P=0.106)


DPP4-INHIBITORS IN THE HOSPITAL SETTING

- Randomized, open-label pilot study of general medical and surgical patients (n=36)
- T2D on diet, any orals, low dose insulin (≤ 0.4 units/kg/day)
- 3 Arms: sitagliptin alone, sitagliptin + glargine, or basal + bolus insulin

RESULTS
- No difference in mean daily glucose
- No difference in number of target glucose readings
- No difference in hypoglycemia
- No difference in LOS
- Less total daily insulin dose and number of injections in the sitagliptin group


CHALLENGES TO ORAL DIABETES THERAPIES IN THE HOSPITAL

Many restrictions to use of orals in the hospital:
- Renal or hepatic impairment (e.g. metformin, sulfonylureas, TZD, SGLT-2)
- Volume overload (TZD)
- Changing nutritional status or malnutrition (insulin secretagogues)
- Contrast dye for imaging or procedures (metformin)
- Slow pharmacokinetic profiles of oral agents infective for rapid changes in glucose and insulin requirements
- Risk of hypoglycemia is unclear in the hospital setting
CURRENT GUIDELINES FOR GLUCOSE TARGETS

• Non-ICU Patients:
  – Premeal glucose targets <140 mg/dL
  – Random blood glucose (BG) <180 mg/dL
  – To avoid hypoglycemia, reassess insulin regimen if BG levels fall below 100 mg/dL
  – Some patients may be maintained with a glucose range below and/or above these cut-points

  Hypoglycemia = BG <70 mg/dL
  Severe hypoglycemia = BG <40 mg/dL

STRATEGIES TO ACHIEVE GLYCEMIC CONTROL IN CRITICALLY ILL PATIENTS

ADMISSION #1: HIP FRACTURE

• 66 year old female with osteoporosis admitted with a hip fracture
• History of T2DM for 12 years, Hypothyroidism, CAD, CKD 3-4
• DM Meds: metformin 1000mg BID, glyburide 5 mg bid, sitagliptin 100 mg QD
• Admission Labs: Glucose 220 mg/dL, Cr= 1.6, A1c = 9.2%
• Underwent ORIF and postoperative glucose is now 330 mg/dL

How should we treat her diabetes?
1. Continue metformin and pioglitazone but increase glyburide dose
2. Discontinue all oral agents and start sliding scale insulin therapy Q 4-6 hours
3. Start a basal (intermediate or long acting) + bolus (rapid acting) insulin regimen

To avoid hypoglycemia, reassess insulin regimen if

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To avoid hypoglycemia, reassess insulin regimen if
KEY CONCEPTS OF EFFECTIVE INSULIN THERAPY

Be Proactive, Not Reactive

- **Basal** insulin
  - Controls hepatic glucose production
- **Food (prandial)** insulin
  - Based on meal carbohydrate content
- **Correction (supplemental)** insulin
  - Treats acute elevation in blood glucose

INITIATING A BASAL BOLUS INSULIN REGIMEN

No clue where to start???

WEIGHT BASED INSULIN DOSING

**INITIAL DOSING FOR BASAL + BOLUS INSULIN REGIMEN**

Choose patients level of insulin resistance (sensitive/average/resistant) and match to patient's weight in kg to find the dose of Lantus and Lispro with meals.
WEIGHT BASED INSULIN DOSING

**Basal Insulin Dosing**
- Basal insulin regimen (let us): 
  - For insulin-naive patients (BMI > 30), use 1 U/kg (oral intake 100mg/dL).
  - Adjust for weight changes:
    - Gain ≥ 10%: +25%
    - Loss ≥ 10%: -25%
  - Adjust for recent weight changes:
    - Increase: +0.3 U/kg/day
    - Decrease: -0.3 U/kg/day
  - Insulin requirements: 0.1 U/kg/day for each 100mg/dL increase in HbA1c.

**Prandial Insulin Dosing**
- Prandial insulin regimen:
  - Basal-Bolus insulin regimen:
    - Basal insulin: 1 U/kg for each 100mg/dL increase in HbA1c.
    - Bolus insulin: 0.1 U/kg for each 100mg/dL increase in HbA1c.

EHR will auto calculate the basal and prandial insulin dosing with weight based dosing option.

CORRECTION INSULIN

ADMISSION #1 – READY FOR DISCHARGE

- Patient has been treated with basal bolus insulin regimen
- Glucose has been between 100-180 mg/dl
- Uncomplicated postop recovery
- Cr is 1.8

What should the discharge regimen be?

**Reassess pre-admission regimen:**
- Outpatient DM Meds: metformin 1000mg bid, glyburide 5mg bid, sitagliptin 100mg daily
CONSIDERATIONS WITH NON-INSULIN DIABETES MEDICATIONS

- **Renal Insufficiency:**
  - Metformin: Cr > 1.5 (eGFR < 60 cc/min) in men and > 1.4 in women for metformin
  - Sulfonylureas (exception of glipizide)
  - Reduce doses for some DPP4 inhibitors, GLP1-RA agonists and SGLT2 inhibitors

- **Hepatic Insufficiency:**
  - Metformin and TZD: LFT’s >2-3x upper normal

- **Volume Overload:**
  - TZDs: Renal failure, liver failure, heart failure

DISCHARGE REGIMENS

What is the A1c?

<table>
<thead>
<tr>
<th>A1c</th>
<th>Preadmission Regimen</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;7%</td>
<td>Continue previous regimen</td>
</tr>
<tr>
<td>7-8%</td>
<td>Increase doses of previous agents or add additional oral or non-insulin agent. If already on max dose of ≥2 oral agents, consider basal insulin</td>
</tr>
<tr>
<td>8-9%</td>
<td>Add basal insulin to previous oral or non-insulin regimen or if already on basal insulin, change to multiple daily injections</td>
</tr>
<tr>
<td>&gt;9%</td>
<td>Multiple daily injections</td>
</tr>
</tbody>
</table>

Other Considerations for Patient Centered Approach:
- Financial
- Patient cognition, literacy, ability to comply
- Risks of hypoglycemia
- Weight management
- Follow up as outpatient

ADMISSION #2: SOB

- 56 year old male admitted to the floor with pneumonia and COPD exacerbation
- History of T2DM for 6 years
- DM Meds: Metformin 1000mg BID, canagliflozin 300mg daily
- Labs: Glucose 190 mg/dL, Cr= 1.0, HgbA1c = 6.7%
- Started on antibiotics and solumedrol 60mg iv daily

How should we treat his diabetes?
1. Continue metformin and canagliflozin
2. Discontinue orals and start sliding scale insulin therapy every 4-6 hours
3. **Start basal + bolus insulin therapy**
INSULIN REGIMENS FOR CORTICOSTEROIDS

- Consider NPH with rapid acting regimens
- Dose basal insulin higher during the day than overnight
- Dose prandial insulin higher towards the end of the day
- May need a ratio of higher prandial than basal insulin (60-70% prandial vs. 30-40% basal)

SUGGESTED INSULIN DOSING FOR STEROID TAPER

<table>
<thead>
<tr>
<th>Prednisone Dosage (mg/day)</th>
<th>Insulin Dosage (U/kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>20</td>
<td>0.4</td>
</tr>
<tr>
<td>30</td>
<td>0.5</td>
</tr>
<tr>
<td>20</td>
<td>0.3</td>
</tr>
<tr>
<td>10</td>
<td>0.1</td>
</tr>
</tbody>
</table>

Consider other comorbid conditions that would increase or decrease insulin resistance and adjust the ratio.

ADMISSION # 3: TRANSFER FROM ICU

- 72 year old female admitted with fever, SOB and hypotension
- Admitted to medical ICU for urosepsis and SIRS
- No history of Type 2 Diabetes but has HTN, Hyperlipidemia, CAD, Gout.
- Labs: Glucose= 225 mg/dL, repeat was 253 mg/dL  HgbA1c = 5.9%  Creatinine = 1.8  AST/ALT = normal
- Managed with pressors, corticosteroids, antibiotics and vent support
- Excellent glycemic control was achieved with intravenous insulin infusion
ADMISSION #3 – CONTINUED

- Over the next few days, the patient improves significantly.
- Pressures are weaned off and steroids are reduced. She is extubated.
- Tube feedings were started and titrated to goal rate
- 24 insulin requirements from insulin infusion while on stable TF rates are 65 units
- Renal and liver function returning to normal
- Ready for transfer to floor on current TF regimen with plans for swallow study in a few days.

What should we do with the insulin regimen?

1. D/C insulin infusion and start sliding scale insulin only
2. Transition to a basal + SC insulin regimen with sliding scale
3. Start metformin 500mg bid and Glyburide 5mg daily

What happened?

Over the next few days, the patient improves significantly.

Rate are 65 units

Options for Insulin Regimen:

1. Glargine/Detemir daily + Rapid Acting Q4 hours
2. NPH Q6 8 hours + Rapid Acting Q4 hours
3. 70/30 Mixed Insulin BID – TID

Sample calculation of transition from insulin drip:

Prior 24 hours intravenous insulin = 65 units
70% = 46 units
NPH 15 units q9 hours with lispro/aspart correction q4 hours.

ADMISSION #3 – CONTINUED

- Several days later the patient passes the swallow evaluation.
- Hydrocortisone is tapered off
- The TF are discontinued at 10 am
- Last NPH dose was at 8 am as scheduled
- At 1 pm, she has a hypoglycemia to 45 mg/dl

What happened?
HYPOGLYCEMIA WITH SUDDEN INTERRUPTION IN CALORIES

- D10% IVF readily available for patients and start at the same rate as the nutritional rate if on TPN or tube feeds
- Continue D10% until tube feeds resumed or effect of long acting insulin is worn off
- **ADJUST THE INSULIN THERAPY OR NOTIFY THE PRIMARY PROVIDER**

SPECIAL REGIMENS FOR CONTINUOUS TPN OR TUBE FEEDS

For patients on continuous tube feeds or TPN, recommend a regimen of NPH Q 8 hours with lispro Q 4 hours.

Special nursing instructions: Start Dextrose 10% IV during any interruption in tube feeds or TPN up to a max of 40 cc/hr. HOLD next insulin dose and notify prescriber for further orders.

ADMISSION # 3 – DISCHARGE REGIMEN

- Blood sugars have been normal without additional insulin on stable oral diet
- Ready for discharge

Does the patient need insulin or oral agents for discharge?

Reminder: Admission HgbA1c = 5.9%
HOSPITAL HYPERGLYCEMIA REQUIRES DISCHARGE FOLLOW UP

- **In those with previously diagnosed diabetes, newly diagnosed diabetes, or elevated A1c**
  - Initiate therapy or revise preadmission regimen as required
- **In those without previously diagnosed diabetes**
  - Differentiation between hospital-related hyperglycemia and undiagnosed diabetes requires follow-up testing (FBG, 2h OGTT, A1c) once metabolically stable using established criteria

ADMISSION #4: HOSPITAL ACQUIRED CONDITION

- 32 year old male admitted for Left femoral-popliteal bypass
- H/o Type 1 DM for >20 years on an insulin pump at home and on admission. HgbA1c was 6.7% on this regimen
- On admission he was placed NPO after midnight and insulin pump was removed and sliding scale was ordered
- On the morning of surgery, patient was found to be confused, tachypneic with shallow respirations
- Labs: Glucose =426, Potassium = 5.6, pH =7.2, Bicarb=14, anion gap of 16, positive serum ketones
  
  What happened???
DANGERS OF SLIDING-SCALE INSULIN REGIMENS

- Sliding Scale Insulin is a reactive therapy → provides supplemental insulin after hyperglycemia occurs
- No basal (long term) insulin coverage which is critical for patients with Type 1 diabetes

Iatrogenic DKA!

DIABETES TECHNOLOGY IN THE HOSPITAL

- Increasing utilization of outpatient technology will follow patients into the hospital
  - Continuous Subcutaneous Insulin Infusion (CSII) or Insulin Pump therapy
  - Continuous Glucose Monitoring (CGM)
- Advantages: less severe glycemic excursions, programmed to avoid hypoglycemia, patient satisfaction
- Disadvantages: not well studied or approved in the hospital, unfamiliarity with non-endocrine trained staff, not proven to be more efficacious in inpatient settings

TYPES OF TECHNOLOGY

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CSII - BASICS

<table>
<thead>
<tr>
<th>Pump Feature</th>
<th>Description</th>
</tr>
</thead>
</table>
| Basal Rates  | Ex: 00:00 0.95 U/h, 06:00 0.5 U/h, 17:00 0.8 U/h | - Rate of continuous infusion of a rapid acting insulin (humalog, aspart, glargine, or regular insulin) 
- Set by time of day 
- Multiple rates throughout the day 
- Can be set to hundredths of a unit per hour |
| Bolus        | Ex: 00:00 10 grams, 08:00 12 grams | - Amount of carbs for a unit of insulin 
- Individualized for each patient 
- Accurate dosing of insulin for the carbohydrates |
| Insulin to carbohydrate ratio (ICR) or Carbohydrate Ratio (CR) | Ex: 00:00 10 grams, 08:00 12 grams |
| Insulin Sensitivity Factor (ISF) or Correction Factor (CF) | Ex: 00:00 50 mg/dl, 12:00 35 mg/dl | - Amount of decrease in glucose per unit of insulin 
- Individualized for each patient |
| Target Glucose | Ex: 00:00 60-120 mg/dl, 12:00 100-130 mg/dl | - Glucose level above which a correction dose is given |
| Insulin on Board (IOB) or Active Insulin Time (AIT) | Ex: 4 hours | - Duration of time between successive correction doses, avoids stacking |

CONTINUOUS SUBCUTANEOUS INSULIN PUMPS (CSII)

- Some small, single center studies have shown that continuing CSII is safe in the hospital
- Standardized hospital protocols, order sets and patient consents are strongly recommended
- Key is to identify that the patient is using their own supplied insulin pump and has mental capacity to continue the therapy
- Protocol should include safety parameters that address the frequency of glucose monitoring, daily pump site and patient assessment, and hypoglycemia treatment

PERIOPERATIVE MANAGEMENT OF CSI

- Retrospective review of patients with CSII preoperatively for elective surgeries
- 49 patients undergoing 57 surgeries
- Protocol in place for CSII management
- Efficacy: 63% had postop CBG of ≤200 mg/dl,
- Safety: No intraoperative or postoperative hypoglycemia <70 mg/dl
- Lower mean postoperative glucose if surgery was less than 120 minutes, more patients met this endpoint
- CSII is safe and efficacious, especially for surgery <120 min

Sabel et al. Endo Prac 2015, 21(11):1269-1276
10/11/2016

**CSII – SURGERIES AND PROCEDURES**
- Plan ahead before elective surgeries
- Can continue CSII during short procedures at discretion of surgeon and anesthesiologist if pump site does not interfere with surgical field
- May use short acting SQ insulin if CSII is held for 1-2 hours.
- If CSII is to be held for > 3 hours, **start basal bolus insulin regimen**
- Can reduce basal rates with the “temp basal” function by a 20-50% of the usual rate

AACE Consensus Panel on Insulin Pump Management Endo Prac 2010 16(5): 746-762

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**CONTINUOUS GLUCOSE MONITORING (CGM)**
- Currently not FDA approved in the hospital setting
- Most studies are in ICU patients or postoperative patients
- Accuracy is a concern due to interference with medications (e.g. TYLENOL) and physiological changes during acute illness (pH, volume overload, etc.)
- No guidelines or protocols available to incorporate this data into management
- More research is needed in the inpatient setting

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**CHALLENGES TO GLYCEMIC CONTROL IN THE HOSPITAL SETTING**
BARRIERS IN THE HOSPITAL

• Diabetes/hyperglycemia often overlooked on admission and throughout the hospitalization if it is not the primary diagnosis
• Hypoglycemia feared and often over-treated
• Lack of familiarity with the increasing types of diabetes therapies currently available
• Traditional sliding scale protocols continue to prevail due to ease and lack of education

BARRIERS IN THE HOSPITAL

• Increased workload on nursing
• Timing of insulin with the glucose check and meals may still be problematic
• Lack of coordination between departments, e.g., nutrition, radiology, nursing, etc.
• Frequently changing nutritional status, medications and organ function that affects glycemic control
• Complexity of individualized dosing + need to make daily adjustments

CONDITIONS PREDISPOSING PATIENTS TO HYPOGLYCEMIA

Advanced age
Sepsis/shock
Malnutrition
Burns
Gastrointestinal malabsorption
Cerebrovascular accident
Hypoglycemia unawareness
Altered Mental Status
Congestive heart failure
Renal insufficiency
Adrenal/pituitary insufficiency
Liver disease
Pregnancy
Alcoholism
Polypharmacy (drug interactions)
INPATIENT DIABETES

TEAMS

Multidisciplinary experts in diabetes are needed to form an effective team:

1. Clinician: physician or physician extender
2. Nurse
3. Diabetes Educator
4. Nutritionist
5. Pharmacist

RESOURCES

American Association of Clinical Endocrinology Diabetes Resource Center http://resources.aace.com

THANK YOU FOR YOUR ATTENTION!